

Remarks:

Applicant has carefully studied the non-final Examiner's Action mailed January 12, 2009. These explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is now believed to be in condition for allowance.

Applicant responds to the outstanding Action by centered headings that correspond to the centered headings employed by the Office, to ensure full response on the merits to each finding of the Office.

Interview

Applicant acknowledges the Interview Summary prepared by Examiner Angell summarizing the telephonic interview on Wednesday, January 21, 2009. Applicant thanks Examiner Angell and Supervisory Examiner Schultz for their consideration and suggestions.

Status of the Claims

Claims 1, 2, 6, 8, 10, 21, 22 and 24-28 were pending in the Office Action mail dated January 12, 2009. Claim 24 and 26 are canceled in the present response. Claims 6 and 25 are amended to recite that "the electric field *is* a pulse selected from the group of waveforms...", as opposed to "the electric field *comprises* a pulse selected from the group of waveforms...", thereby making the nature of the electric field explicit within the context of claims 1 and 21. None of the other pending claims are amended, canceled or withdrawn in the present response. Therefore, claims 1, 2, 6, 8, 10, 21, 22, 25, 27 and 28 are currently pending and under examination.

Claim Rejections – 35 USC § 103(a)

Claims 1, 2, 6, 8, 10, 21, 22 and 24-28 stand rejected under rejected 35 USC § 103(a) as being unpatentable over U.S. Patent No. 6,055,453 to Hofman ("Hofman") in view of U.S. Patent 6,678,558 B1 to Dimmer et al. ("Dimmer"). Applicant traverses this rejection on the grounds that (1) one or more elements are missing from the cited combination (i.e. Dimmer does not resolve the deficiencies of Hofman with respect to the invention as claimed) and (2) that the cited art, in combination with state of the art and the knowledge of one of ordinary skill in the art

at the time of the invention, would not have provided one of ordinary skill in the art with a motivation to make the invention as claimed.

In rejecting claims under 35 U.S.C. § 103(a), it is incumbent upon the Office/Examiner to establish a factual basis to support the legal conclusion of obviousness.¹ In so doing, the Examiner must make the factual determination set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). In *Graham* the court held that the obviousness analysis is based upon several factual inquiries: “[(1)] the scope and content of the prior art are to be determined; [(2)] differences between the prior art and the claims at issue are to be ascertained; and [(3)] the level of ordinary skill in the pertinent art resolved.”² “[T]he Examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability.”³ “All words in a claim must be considered in judging the patentability of that claim against the prior art.”⁴ Furthermore, “ ‘[t]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness’ ...”⁵

Dimmer does not resolve the deficiencies of Hofman

The combined references fail to establish a *prima facie* case of obviousness as outlined by MPEP 2142 for reasons including that the combined references fail to teach or suggest all claim limitations (see also MPEP 2143.03). In particular, Dimmer in view of Hofman fail to teach or suggest a method including the “appl[ication] of a continuous electric field in the range of 1mV/cm to 200V/cm to the target tissue for a duration of 200ms to 20 minutes ...” The Office recognizes as much with respect to Hofman when it is stated that “Hofmann does not teach applying the pulse for a duration of longer than 100ms.”⁶ Therefore, Hofman does not supply the teaching of a duration of 200ms to 20 minutes as in claim 1.

Presumably, then, the Office relies on the teachings of Dimmer for this element. However, the office action seems to only tangentially address the issue of pulse for a duration of

¹ *In re Fine*, 837 F.2d 1071, 1073 (Fed. Cir. 1988).

² *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). See also *KSR Int'l v. Teleflex Inc.*, 127 S.Ct. at 1734.

³ *In re Oetiker*, 977 F.2d. 1443, 1445 (Fed. Cir. 1992).

⁴ See MPEP 2143.03 – All Claim Limitations Must be Considered – citing in *re Wilson* “ ‘All words in a claim must be considered in judging the patentability of that claim against the prior art.’ ” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).”

⁵ *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007) quoting *In re Kahn*, 441 F. 3d. 977, 988 (Fed. Cir. 2006).

⁶ Office Action mail dated December 31, 2008 at page 3, final sentence.

longer than 100ms when discussing Dimmer.⁷ The Office does provide an excerpt from Dimmer where the Office states:

Importantly, Dimmer teaches: ... As the electric field increases, the total electroporation signal duration can be decreased in order to prevent excessive amounts of energy from being delivered to the treatment site 30. The total electroporation signal duration is preferably less than about 10 seconds, more preferably about 30 μ s-10 seconds, even more preferably about 30 μ s-1ms and most preferably about 50 μ s-400ms. (See column 20, lines 38-44);

Therefore, the reasonable conclusion from the assertions made on pages 3-4 of the Office Action is that the Office is relying on Dimmer for the teaching applying the pulse for a duration of longer than 100ms, which the Office asserts is lacking in Hofman.

However, the issue of Dimmer teaching or suggesting a single electric pulse of a duration of 200 ms or longer has been adjudicated, with the Board finding that Dimmer did not provide such a teaching or suggestion. In particular, the Board stated:

We disagree with the Examiner that Dimmer teaches a single electric pulse of 200 ms (*see* Ans. 10). At no point does Dimmer teach a pulse of such length and Dimmer teaches "a pulse duration of less than about 50 μ s, more preferably have a pulse duration of less than about 12.5 μ s and most preferably a pulse duration of less than about 5 μ s" (Dimmer, col. 10, ll. 12-16). Dimmer's claims support this conclusion, with claim 6 of dimmer claiming a range of pulse duration from 2 to 50 μ s (*see* Dimmer, col. 32, ll. 22-23, claim 6). While claim 4 of Dimmer teaches a method with as little as a single pulse, Dimmer never suggests that the length of the pulse should be more than 50 μ s, only that if there is a time delay between pulses, that time delay can be 5 to 200 ms (*see* Dimmer, col. 32, ll. 17-19, claim 4).

Thus, the Board found that not only did Dimmer not teach a single electric pulse of a duration of 200 ms or longer, "Dimmer never suggests that the length of the pulse should be more than 50 μ s..." Accordingly, Dimmer fails provide a teaching or suggestion to overcome the shortcomings of the primary reference, Hofman.

As a final matter with regard to Hofman, it should be noted that in the first paragraph of page 7 of the Office Action dated November 29, 2005 the Office states that "Hofman does not teach applying the pulse for a duration of longer than 100 ms. As such, amending the claims such that they are limited to applying the pulse for a duration of 200 ms to 20 minutes would obviate this rejection." While the rejection that was referred to was one under 35 U.S.C. 102(b), it would only be reasonable to conclude that the Examiner had further considered the implications of Hofman vis-à-vis a rejection under 35 U.S.C. 103(a).

⁷ Office Action mail dated December 31, 2008 at page 4.

Hofman in view of Dimmer does not provide a motivation make the invention as claimed

The claims are drawn to “[a] method for facilitating the delivery of a desired molecule into a target tissue ...” The method includes the application of a continuous electric field to the target tissue for a duration such as between 200 ms and 20 minutes. (e.g. claims 1 and 21) Application of the field effects a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of the cell. Hofman does not teach such a method, as indicated by the Office.⁸ Nevertheless, it is asserted in the office action that one would be motivated to modify the teachings of Hofman by applying the teachings of Dimmer.⁹ To bolster this line of reasoning the Office states:

Hofmann provides an explicit teaching that when low electric fields are used, longer pulses should be used. Specifically Hofmann teaches, “[I]t is preferred that when the electric field is low, the pulse length is long.” (See column 10, lines 37-39). Therefore, Hofmann provides a motivation to use low electric fields for longer durations of time. Furthermore, since Hofmann teaches that applying an electric field within the claimed range for a duration of 100ms is sufficient to change the porosity of a cell membrane to allow entry of a molecule into a cell, it would be expected that increasing the length of the pulse to more than 200ms and up to 10 seconds would also be sufficient to facilitate entry of a molecule into a cell.

A couple of points can be made about the excerpt. First, the Office explicitly states that Hofman does not teach a pulse for a duration for longer than 100ms, but the Office cites to Dimmer to satisfy this shortcoming. However, no clear case is made as to how Dimmer resolves the deficiency in Hofman with respect to not teaching a pulse duration in excess of 100 ms. It is submitted that Dimmer teaches away from applicants’ inventions, as stated previously by Applicant on pages 12-13 of their Appeal Brief. Therefore, one of skill in the art, when modifying the teachings of Hofman by applying the teachings of Dimmer, would be motivated to adopt pulses of increasingly short duration to thereby reduce patient discomfort. In summary, Dimmer does not add to the teachings of Hofman with respect to a rejection of the claims at issue under 35 U.S.C. 103(a).

The second point regards the assertion that “Hofmann provides an explicit teaching that when low electric fields are used, longer pulses should be used. Specifically Hofmann teaches, ‘[I]t is preferred that when the electric field is low, the pulse length is long.’ (See column 10, lines 37-39). Therefore, Hofmann provides a motivation to use low electric fields for longer durations of time.” It is respectfully submitted that such a statement merely recognizes an inverse

⁸ Office Action mail dated December 31, 2008 at page 3 - “Hofmann does not teach applying the pulse for a duration of longer than 100ms.”

⁹ Office Action mail dated December 31, 2008 at page 4, final paragraph.

relationship between field strength and duration. The corollary would be saying when the electric field is high, the pulse length is short. However, this is not a call by Hofman to adopt longer pulse durations over shorter pulse durations. Furthermore, there exists a fundamental question when subjective/relative terms such as low and high or short and long are offered. What are the limits of such a term? More precisely, what constitutes a "long" pulse length with respect to the teachings of Hofman? Would anything longer than a 1 ms pulse length be long to Hofman?

In light of the foregoing, it is respectfully submitted that Hofman in view of Dimmer does not provide a motivation make the invention as claimed. Nor does Hofman, alone, provide such a motivation. Moreover, one or more elements are missing from the cited combination (i.e. Dimmer does not resolve the deficiencies of Hofman with respect to the invention as claimed). It is therefore respectfully requested that the Office withdraw the rejection of claims 1, 2, 6, 8, 10, 21, 22 and 24-28 under rejected 35 USC § 103(a) as being unpatentable over U.S. Patent No. 6,055,453 to Hofman in view of U.S. Patent 6,678,558 B1 to Dimmer et al.

Conclusion

For the reasons cited above, Applicant believes that claims 1, 2, 6, 8, 10, 21, 22, 25, 27 and 28 are patentable and in condition for allowance.

If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (813) 925-8505 is requested.

Very respectfully,
SMITH & HOPEN

Dated: April 13, 2009

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CERTIFICATE OF ELECTRONIC TRANSMISSION TRANSMISSION
(37 C.F.R. 2.190(B))

I HEREBY CERTIFY that this Amendment K is being electronically transmitted to the United States Patent and Trademark Office through EFS Web on April 13, 2009.

Date: April 13, 2009

/lauren reeves/
Lauren Reeves